1999 Epidemiological Report on Tuberculosis

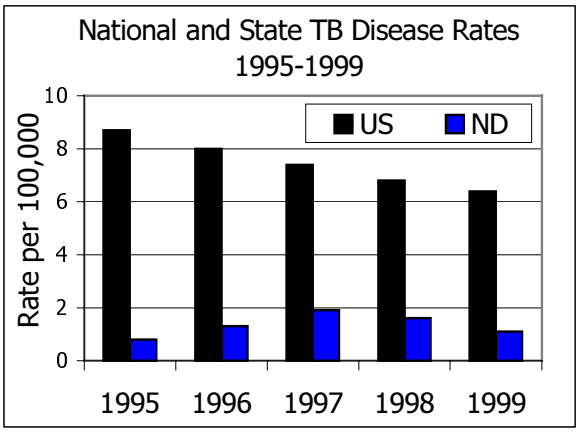
North Dakota Department of Health
Division of Disease Control

TB in North Dakota

TB in North Dakota – 1999

North Dakota had seven cases of tuberculosis (TB) disease reported in 1999. With an incidence rate of 1.1 per 100,000, North Dakota continues to be well below the national rate (Figure 1).

Figure 1



TB was reported in four of North Dakota's 53 counties. One case was reported in Burleigh County, two in Cass, three in Grand Forks and one in Sioux.

Three cases were pulmonary, three were extra-pulmonary (occurring in cutaneous tissue, the prostate and the pleural space) and one was pulmonary/extra-pulmonary (occurring in both the lung and genitourinary system).

TB case ages ranged from 18 to 82, with a mean and median age of 61 and 64 respectively. One case was black, five were white and one was Native American.

Risk factors associated with TB in 1999 included being homeless, being foreign-born and belonging to a high-risk racial/ethnic group. Other factors included reactivation of prior disease and prior TB infection resulting in TB disease (due to decreased immune response resulting from age and/or contributing underlying medical conditions). No deaths resulting from TB were reported in 1999.

Due to the lengthy medication regimen for active disease, treatment is ongoing for five of the seven cases.

A Five-Year Overview of TB in North Dakota

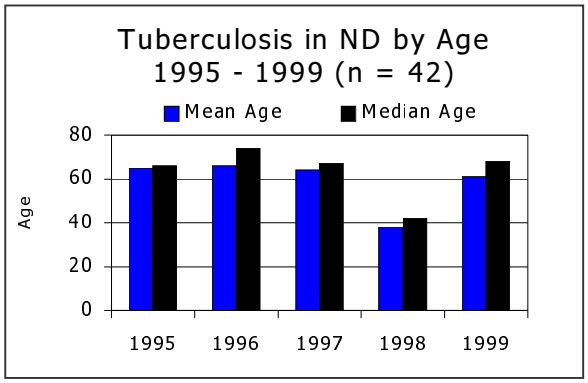
North Dakota has a low-incidence of TB, making it difficult to determine disease trends based on annual data. TB trends can be identified more easily if data from a five-year period is analyzed.

Over the past five years, 42 cases of TB have been diagnosed in North Dakota (Jan. 1, 1995, through Dec. 31, 1999). There have been five to 12 cases reported each

year, an incidence rate of between 0.8 and 1.9 per 100,000.

Of the 42 cases, 30 were pulmonary (71%), 11 were extra-pulmonary (26%) and one was pulmonary/extra-pulmonary (2%). Fifty-two percent of the TB cases were age 60 or above. The mean and median ages of TB cases over the past five years were 58.0 (range = 38.7 to 64.8) and 64.5 (range = 42.0 to 69.0) respectively. (Figure 2)

Figure 2



As shown in Figure 2, the mean and median ages in 1998 were significantly lower than in other years. This is due to the diagnosis of disease in three children, all younger than age 10.

Risk factors associated with TB were multiple, although an increase in the state's racial/ethnic populations over the years directly affected the number of TB cases reported in these racial/ethnic groups. (Table 1)

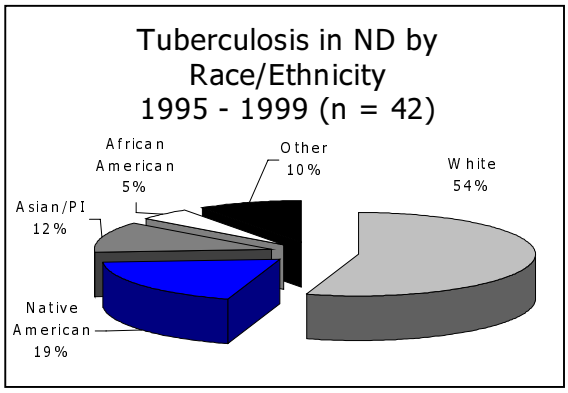
Table 1

Race	1980	1998	% Change
White	625,557	598,791	-4.3
Native American/ Alaskan	20,158	30,108	49.4
Asian/Pacific Islander	1979	5344	170.0
Black	2568	4001	55.8
Hispanic*	3902	6999	79.4

*Hispanic origin can be of any race
Source: N.D. State Data Center, 1998 Estimates

North Dakota's population in terms of race/ethnicity consists primarily of whites (93.96%), followed by Native Americans (4.61%), Asians (0.80%) and blacks (0.63%). The race/ethnicity of TB cases over the past five years reflects the state's population, with the majority of TB cases occurring in whites, followed by Native Americans, Asians and blacks. (Figure 3)

Figure 3



Drug Resistant TB

Drug resistant TB (DR-TB) is present in North Dakota. Table 2 depicts the DR-TB and multi-drug resistant TB (MDR-TB) over the past five years.

Table 2

DR-TB and MDR-TB North Dakota 1995-1999					
	1995	**1996**	**1997**	**1998**	**1999**
Drug Resistance					
Ethambutol	0	0	0	1	0
Isoniazid	0	1	0	0	0
Streptomycin	0	0	0	0	0
Multi-Drug Resistance	1*	0	0	0	0

*INH and Streptomycin

DR-TB and MDR-TB present difficult problems for TB control because treatment of disease and infection in contacts must be individualized based on the individuals'

medication history and drug susceptibility studies.

Latent TB Infection

Latent TB infection (LTBI), formerly referred to as TB infection, occurs when individuals are infected with *M. tuberculosis* bacteria through direct exposure to active disease. People with infection do not have active disease. Clinical findings in LTBI normally include a positive tuberculin skin test (TST), absence of symptoms and a negative chest x-ray.

The number of TB infections reported in North Dakota has increased by 24 percent since 1995. The number of individuals who received or are receiving medication for LTBI over the past five years is shown in Table 3.

Table 3

1995	1996	1997	1998	1999
341	248	255	426	450

The data in Table 3 includes only those who are TB infected and who receive medication. There are many individuals with LTBI who, after consultation with their physician, are not deemed candidates for prophylactic treatment.

Summary

There are two notable trends in the epidemiology of TB in North Dakota.

1) The majority of disease occurs in the 60 and older age group. (Table 2)
2) The increase in TB among racial/ethnic groups is directly correlated to the increase in population among these groups. (Table 1 and Figure 3)

It is important to remember, however, that with North Dakota's low incidence of TB, the demographics of just one or two new cases can significantly alter the epidemiological profile of the disease. This makes it difficult to determine actual trends. This is well demonstrated in 1998 data (Table 2), where the diagnosis of disease in children younger than age 10 decreased the mean and median ages by about 20 years.

TB control in North Dakota is accomplished through collaborative efforts between health care providers and state and local health departments. Each reported TB case is monitored closely to ensure appropriate treatment of disease, contact investigation with appropriate follow-up for LTBI and completion of therapy for both LTBI and TB disease.

Did You Know?

About one-third of the world's population is infected with *M. tuberculosis*.

TB Resources

Tuberculosis Website
Please visit this website at:
www.health.state.nd.us/ndhd/prevent/disease/tb

Core Curriculum 2000
A link to this document is available on the TB Website

Upcoming Events

Annual TB Workshop
May 4, 2000 (Fargo, N.D.)
May 5, 2000 (Minot, N.D.)
* For details, please visit the TB Website or call the TB Program at 701.328.2377.

2000 National TB Controllers Workshop
Aug. 30 – Sept. 1, 2000 (Atlanta, Ga.)

Mycobacterium bovis in North Dakota

Mycobacterium bovis is the bacteria that causes bovine (ruminate mammals; i.e., cows, elk) TB. *M. bovis* belongs to a subset of mycobacterium that includes *M. tuberculosis*, the bacteria that causes TB in humans.

Bovine TB can be transmitted both from animals to humans and from humans to animals. Animals and humans can contract the disease by drinking raw milk from infected animals; however, the most common route of transmission is through respiration. Invisible droplets containing TB bacteria are expelled by infected animals and then inhaled by susceptible animals or humans. No other TB organism has as great a host range as bovine TB, which can infect all warm-blooded vertebrates.

Clinically, disease resulting from *M. bovis* is difficult to distinguish from disease resulting from *M. tuberculosis*. Treatment is similar except that *M. bovis* displays an innate resistance to the antibiotic Pyrazinamide (PZA). So, treatment with two- or three-drug regimens of iosaniazid, rifampin, ethambutol and streptomycin for nine to 12 months is recommended.

M. bovis Found in a Dairy Herd

Background

On Feb. 17, 1999, the North Dakota state veterinarian's office received notification than an animal with lesions consistent with TB had been traced to a dairy herd in the state. The cow with the lesions was found during routine United States Department of Agriculture (USDA) inspection at a Minnesota slaughter house. On February 23, the owner of the dairy herd was contacted and skin testing on the remaining cattle in his herd was initiated. A total of 115 animals were tested; 54 (47%) tested negative and 61 (53%) tested positive. The USDA purchased four of the cows that tested positive from the owner and shipped them to the State Veterinary Diagnostic Laboratory for postmortem exam for TB. Initial testing showed three of the four animals had histologic lesions consistent with TB and one with acid fast organisms. The remaining 57 cattle that tested positive were subjected to comparative testing to distinguish between *M. avium* and *M. bovis* infection in cattle. Results from the comparative testing revealed 15 were positive for *M. avium*, 11 were *M. bovis* suspects, and 31 were *M. bovis* reactors.

On March 10, the State Board of Animal Health declared the herd to be TB infected. The entire herd was destroyed and a quarantine of about a five-mile radius was placed on the area surrounding the infected dairy herd. The quarantine restricted movement of livestock within or out of the area unless a permit was issued by the state veterinarian. With assistance from the USDA, every herd in the quarantined area was tested for TB, a process that took several months to complete. In addition, extensive investigations were undertaken to trace sales of cattle from the infected herd to other areas, as well as to ascertain the source of infection.

Human Implications

The North Dakota Department of Health (NDDoH) was notified by the state veterinarian on March 2 about possible human exposures to *M. bovis* in a dairy herd. The NDDoH began working closely with the North Dakota Department of Agriculture to determine risk factors and exposed populations. The owner of the dairy herd sold milk from the cattle to a local cheese processing plant. The plant did not pasteurize the milk product, but shipped it out-of-state where further processing was done. Individuals considered at-risk for *M. bovis* exposure included those who had ingested or handled unpasteurized dairy products, as well as those who had direct contact with infected cattle.

The following recommendations were provided for suspected exposures*:*

- Exposed people received a baseline tuberculin skin test (TST). An induration of 5 mm was considered positive. Those people who tested negative were retested within 10 to 12 weeks after the last exposure.

- All exposed people with positive TST results were screened for symptoms and received a physical exam and chest x-ray.

- Children who were exposed and TST positive, and children age 4 and younger who were exposed (regardless of TST results) received a chest x-ray. Children with positive (5 mm) reactions received iosaniazid (INH) prophylaxis. Children age 4 and younger received INH prophylaxis until a negative result was confirmed by a retest administered 10 to 12 weeks following last exposure.

- INH prophylaxis for six to nine months was prescribed for those exposed and TST positive (5 mm), children included.

A total of 107 individuals were skin tested. Of those, 101 (94%) tested negative, and six (6%) tested positive. Of the six individuals who tested positive, two were foreign-born individuals who had never been tested, one was an elderly person who may have been exposed to pulmonary TB as a child, another was exposed to the dairy herd, one worked at the plant and one had worked with the infected herd. Two of the six individuals consumed unpasteurized dairy products. It was concluded that there was no definitive correlation between the infected people and the infected cattle.

Testing of cattle in the quarantined area was completed. All 31 of the herds tested were negative. Only the one initial herd has been identified as infected.

Did You Know?

North Dakota has been declared free from bovine TB since 1976. The state was able to retain its TB-free status even after the infected herd was identified in 1999. This was possible because the source herd was destroyed and no other infected herds were identified.

The Death of Eleanor Roosevelt: Missed Diagnosis or Inevitable Outcome?

Adapted from a Washington Post article dated Feb. 8, 2000, by Barron H. Lerner, MD, PhD, Assistant Professor, Columbia University

I first heard the story about Eleanor Roosevelt's death when I was a medical student at Columbia-Presbyterian (now New York Presbyterian Hospital). The "First Lady of the World" had died at Colombia-Presbyterian, one of the country's most prestigious medical institutions, of miliary TB, a curable disease. Imagine my curiosity, then, when I learned that Eleanor Roosevelt's medical record was available to the public, sitting in a box at the Franklin D. Roosevelt Library in Hyde Park, N.Y. Remarkably, no one had examined Roosevelt's medical record until now.

In April 1960, at age 75, Eleanor Roosevelt was found to have anemia, an insufficient number of red blood cells (RBC's). Until this time, she had maintained a remarkably vigorous schedule, traveling around the world to publicize the plight of the disadvantaged. To learn the cause of the anemia, her physician and close friend, Dr. David Gurewitsch, referred her to a hematologist for a bone marrow aspiration. This test, which involves the removal of cells from a patient's pelvic bone, revealed that Roosevelt had aplastic anemia. Her bone marrow was simply not producing enough RBCs. Despite her anemia, Roosevelt continued to travel, remarking that she was "too busy to be sick." But, in September 1961, her anemia worsened and she required two blood transfusions. While receiving the blood, Roosevelt suffered the first of many transfusion reactions, with a high fever and chills. By April 1962, her anemia had worsened and she developed an inadequate number of white blood cells, which fight infection, and platelets, which enable blood to clot. Given this development, Gurewitsch decided to treat the aplastic anemia and low platelet count by prescribing prednisone; known to stimulate the bone marrow to produce more cells but also to weaken the immune system.

Despite prednisone therapy, Roosevelt continued to require periodic blood transfusions during the summer of 1962. On August 3, she developed a post-transfusion fever of 105 degrees and was admitted to Columbia-Presbyterian. Upon admission, she told her doctors that she had been experiencing a cough for several weeks. Given the combination of fever and a cough, TB disease was considered as a possible diagnosis.

TB typically causes an infection in the lung demonstrated by localized density on a chest x-ray. However, Roosevelt's x-ray was clear, except for old scars indicating past exposure. When her fever dissipated after five days, she was discharged but continued prednisone therapy to treat the anemia.

On September 26 she was readmitted to the hospital. Her condition continued to deteriorate. The fever persisted and now she was passing blood in her stool. Roosevelt clearly had something more than just aplastic anemia. Doctors termed her case a "fever of unexplained origin."

The Death of Eleanor Roosevelt (cont.)

Roosevelt's doctors revisited the possibility of TB. But, now they were focusing on a rarer form of the disease, miliary TB, which occurs when TB bacteria spread through the bloodstream to the lungs, bone marrow and other organs. Because Roosevelt had evidence of an old TB infection, it was possible that her debilitated condition, plus the prednisone, had weakened her immune system and allowed the disease to reactivate and spread. The diagnosis of miliary TB often was made by chest x-ray, which typically showed tiny, discrete nodules the size of millet seeds – hence, the name miliary. In Roosevelt's case, the x-ray showed an "ill-defined nodularity," but not one that looked like miliary TB. To pursue the diagnosis of TB, doctors performed another bone marrow aspiration on September 27, this time to look for the characteristic bacteria of the disease. When they found none, they sent the specimen to the laboratory for culture, a process that would take four to six weeks.

After the aspiration, her physicians did decide to treat her empirically with two antimicrobials, iosaniazid and streptomycin. Aside from a five-day period during which the streptomycin was stopped, due to a question of a drug allergy, Roosevelt received a two-drug treatment for TB until she died. Although the fever briefly waned after the medication was begun, it returned within five days. By October 12, it again reached 105 degrees.

Roosevelt was increasingly unhappy about being hospitalized. Prior to her August admission, Roosevelt had made Gurewitsch promise that she would not die in the hospital. Her children, notably her daughter Anna, agreed, and on October 18, she was discharged. The Columbia physicians had been unable to make a definitive diagnosis. Her doctors agreed her prognosis was poor, but planned to follow her closely at home. The former First Lady's illness remained a mystery until October 26, one week after her discharge. On that day, the bone marrow culture grew TB organisms, suggesting that the old dormant infection had indeed reactivated and spread throughout her body. On November 4, Roosevelt suffered an apparent stroke that left her comatose. She died on Nov. 7, 1962. She was 78 years old.

On December 12, members of the Columbia-Presbyterian community attended a clinical pathological conference to present Roosevelt's case. Her TB had been widespread with a remarkable amount of bacteria found throughout her body, including her lungs, liver, kidneys and brain. The characteristic collections of cells and proteins known as granulomas, that most patients produce in order to fight off the infection, were almost entirely absent. The final diagnosis on the autopsy record was "disseminated TB acutissima," an especially severe and rarely seen form of miliary TB. Doctors hypothesized that Roosevelt had been unable to effectively combat her disease in part due to the prednisone treatment. But the story does not end here.

The Columbia laboratory also discovered that Eleanor Roosevelt's strain of TB was resistant to the two drugs she had received. That is, neither the iosaniazid nor the streptomycin were effective in treating her infection.

Shortly after drugs had been introduced to treat TB in the 1940s, physicians had learned that bacteria could develop resistance. This situation most often occurred when a patient took medications erratically. But people could also develop

The Death of Eleanor Roosevelt (cont.)

drug-resistant TB through contact with other individuals with infectious, drug-resistant disease. In Roosevelt's case, therefore, she most likely had not undergone a reactivation of old TB but had probably come into contact with someone with active, drug-resistant disease. On prednisone, which increased her susceptibility, she had become reinfected with a drug-resistant strain of TB. Nothing could have been done to save her.

Roosevelt almost certainly had disseminated TB when she entered Columbia-Presbyterian in August 1962. Her physicians might have more aggressively pursued the diagnosis during her final admission by performing a bone marrow biopsy, which involves removing actual tissue, as opposed to an aspiration. But, in practice, making such a diagnosis remained difficult. Reports in the literature suggest that physicians diagnosed miliary TB prior to death in only 25 percent of cases.

The severe form of the disease seen at Roosevelt's autopsy was even harder to diagnose during life because no granulomas were produced. Moreover, as the medical record revealed, Roosevelt's physicians had treated her for TB even as they pursued dozens of other possible disease etiologies. And, as Gurewitsch suggested, the fact that the bacteria turned out to be drug-resistant did indicate that her disease was almost certainly untreatable at that time.

Did you Know?

Vivien Leigh, (1913-1967), English actress (Scarlet O'Hara from *Gone With the Wind*) developed TB at the age of 31. Leigh denied treatment, including newly available antibiotics and died of the disease at age 53.

Two-Step Tuberculin Skin Testing

Why Perform Two-Step Skin Testing?

The two-step test is designed to detect individuals with past TB infections, who may have diminished skin test reactivity. The first skin test administered may not be positive, but helps the body "remember" *Mycobacterium tuberculosis.* The second skin test evokes a positive response because the body now identifies and reacts to the purified protein derivative solution. The second (boosted) response is the valid baseline for the individual.

Two-step skin testing can help to avoid problematic situations. For example, an employee (who was infected with TB as a child) had not had a skin test in a long while, and had a negative TB skin test at hire. One year later, the employee was tested as part of routine employee TB surveillance, and developed a 16 mm induration. There is no way to tell if this is a skin test conversion representing new infection or a boosted reaction from old infection. A two-step test at the time of hire would have prevented this dilemma.

When Should a Two-Step Skin Test Be Done?

Use a two-step test for new employees or volunteers who will be routinely tested, and who:

- Have never been tested or have no documentation of being tested, or
- Do not remember being tested, or

- Tested negative more than 12 months ago.

Is Two-Step Skin Testing Cost Effective?

Two-step testing will allow you to establish employee baseline test results, TST conversion rates, and more accurately assess facility risk. It will reduce the likelihood that a boosted reaction is interpreted as a new infection, which can result in unnecessary investigation, prophylactic treatment and employer/employee expense. While groups with a high prevalence of TB infection will particularly benefit from two-step testing, facilities with lower boosting rates will find it just as cost effective.

Latent Tuberculosis Infection

CDC Recommendations for Treatment of LTBI

- Without prophylaxis, approximately 10 percent of people with LTBI will develop active TB in their lifetime. For people co-infected with HIV, the risk of developing TB disease is 10 percent per year. The risk also is higher for children, newly infected people, and those with certain immunosuppressive medical conditions.
- Adequate therapy for LTBI reduces the likelihood of developing disease by up to 80 percent. Incomplete therapy confers little benefit; thus, prophylaxis should be initiated only if completion of the regimen is likely.
- All asymptomatic people younger than age 35 with TB infection and a normal chest x-ray are candidates for treatment of LTBI.
- High-priority candidates for treatment of LTBI, regardless of age, include people with known or suspected HIV infection, close contacts of people with infectious TB, people with chest x-ray results indicative of old healed TB and who have not received adequate treatment, injection drug users, people with certain medical conditions (e.g., diabetes mellitus, end stage renal disease, immunosuppressive therapy), and people whose TST results have converted from negative to positive within the past two years.
- For most people 35 years of age or older without any of the risk factors described above, the risk of INH-induced hepatotoxicity exceeds the risk of developing TB; therefore, prophylaxis is not typically recommended.
- Rule out active TB before initiating prophylactic therapy. Asymptomatic people with a negative chest x-ray result usually can be considered free of active TB disease. Consider the possibility of extra-pulmonary disease, when indicated. Defer prophylaxis until all diagnostic tests for TB have been completed.
- Recommended treatment for LTBI consists of INH 300 mg daily for six to nine months. Children should be treated for nine months at a dosage of 10 to 20 mg/kg (maximum 300 mg). Alternative regimens are available for people who cannot tolerate INH and for contacts exposed to INH-resistant TB. All people receiving INH should be monitored monthly for symptoms of hepatotoxicity and for adherence to the regimen. People 35 years of age or older and those with risk factors for hepatotoxicity should receive baseline liver enzyme testing (i.e., AST) prior to starting INH,

monthly during therapy, or if symptomatic.
- No more than a one-month supply of INH should be dispensed to the patient at a time.
- Medication for treatment of LTBI can be obtained at no cost through the TB Program by calling 1.800.472.2180.

Treatment of LTBI in Special Situations

- Directly observed preventative treatment (DOPT) should always be used with intermittent dosing regimens (e.g., bi-weekly and tri-weekly regimens).
- DOPT also should be used when operationally feasible, especially with two-month preventive therapy regimens and in some special settings (e.g., in some institutional settings, in some community outreach programs, and for some people who are candidates for preventive therapy because they are household contacts of patients with TB disease who are receiving home-based therapy).
- For all people who are known to be contacts of patients with INH-resistant, rifamycin-susceptible TB, a two-month preventive therapy regimen of rifamycin (rifampin or rifabutin) and PZA is recommended. For patients with intolerance to PZA, a four- to six-month regimen of a rifamycin (rifampin or rifabutin) alone is recommended.
- In general, the recommended preventive therapy regimens for people likely to be infected with a strain of *M. tuberculosis* resistant to both INH and rifamycins include the use of a combination of at least two antituberculosis drugs that the infecting strain is believed to be susceptible to (e.g., ethambutol and PZA or levofloxacin and ethambutol). The clinician should review the drug-susceptibility pattern of the *M. tuberculosis* strain isolated from the source-patient before choosing a preventive therapy regimen.
- For HIV-infected children who are candidates for TB preventive therapy, a 12-month regimen of INH administered daily is recommended by the American Academy of Pediatrics.

Two-Drug Regimen for Treatment of LTBI

Taken from MMWR October 30, 1998/Vol.47; No. 42

In October 1998, CDC approved the use of a two-month regimen of daily RIF and PZA (2RZ) as an alternative to six, nine or 12 months of INH for LTBI in HIV-positive people. CDC has been expanded this recommendation to include the use of 2RZ in all people with LTBI for whom preventive therapy is indicated.

However, the cost of 2RZ is significantly higher than the standard INH regimen. Therefore, the state health department will supply medication for 2RZ only in certain situations; for example, an individual with LTBI in a correctional facility who will be in the facility for less than six months or an individual who is unable to tolerate INH and has significant risk factors for developing disease (e.g., recent exposure to an infectious case of TB, immunosuppressed and in need of prophylactic treatment).

Prior approval from the health department is required before the medication will be supplied. Other situations may occur where treatment with 2RZ would be appropriate. Please call the state health department to discuss these situations as they arise.

Model TB Centers

Model TB Centers were established in response to the resurgence of TB in the United States. These centers are federally funded and were developed to decrease morbidity through diagnostic, treatment and prevention programs; to create interaction among clinical and research scientists with a prime interest in TB; to develop and apply diagnostic, therapeutic, behavioral, preventive and educational modalities for TB; and to provide nationally recognized training to increase the skills related to TB for all health-related professionals. Information about all three TB Centers can be obtained via their internet sites as listed below. In addition, two centers operate phone lines to provide expert consultation to health care providers about TB treatment and control.

New Jersey Model TB Center
Phone: 1.800.4TB.DOCS (1.800.482.3627)
Website: **www.umdnj.edu/~ntbcweb/**

Francis J. Curry National TB Center
Phone: 415.502.4700
Website: **www.nationaltbcenter.edu/**

Charles P. Felton National TB Center
Website: **www.harlemtbcenter.org/**

North Dakota Department of Health
Division of Microbiology

The North Dakota Department of Health, Division of Microbiology (or Public Health Laboratory [PHL]) is prepared to assist in the early detection of TB by reducing laboratory turnaround time for reporting positive smear, culture, identification and susceptibility results. The American Thoracic Society recommends using a laboratory such as the PHL, which examines a minimum of 20 mycobacteriology specimens per week to remain proficient. It is important to find a good, full-service reference laboratory that is both timely and accurate.

Services Available Through North Dakota PHL

- Results of acid-fast stains reported within 24 hours of receipt. Service available Monday through Friday.
- Detection of mycobacteria within two weeks of specimen receipt using the BACTEC 460, a liquid medium automated procedure.
- Identification of *M. tuberculosis* and *M. avium* complex using the Accuprobe is completed within one day once the organism is growing in culture. (Direct DNA amplification testing for smear-positive specimens is being investigated for possible implementation.)
- Susceptibility testing of new *M. tuberculosis* isolates to primary drugs. On average, results are available within three to four weeks of specimen receipt.

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References cited in this report are available upon request.